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EXAMINER	
M	3495.010-12

ART UNIT	PAPER NUMBER
1813	15

18M2/0324
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1300 I STREET, N. W.
WASHINGTON, DC 20005-3315

DATE MAILED: 03/24/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 12/20/94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 11, 13, 15 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-10, 12, 14, 16 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 11, 13, 15 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. 158652; filed on 2/22/88.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure, ie. failing to show how to make and or use the claimed invention.

The claims are drawn to antibodies which bind to a peptides of HIV which are gene products of particular open reading frames (ORFs) of HIV-1. The specification teaches the sequence of a particular HIV-1 genome and suggests potential open reading frames or ORFs. The specification also, in general terms describes the production of antibodies specific for the gene product of these ORFs for diagnostic application. One of ordinary skill in the art would have been forced into undue experimentation in order to make the claimed invention by using the specification for guidance. Certain ORFs can be used in conjunction with each other in order to produce a particular gene product. This form of product expression is called split ORFs. It is now known that certain proteins of HIV are produced as a result of multiple ORFs, ie. this is a feature of the *tat*

protein. Although applicant has deleted out this particular gene product, at the time the invention was made, there remained the unpredictability associated with obtaining a proper protein from a single ORF. Very little was known about the gene products encoded by the HIV ORFs at the time the invention was made. In fact, there was no indication that HIV gene products could be effectively expressed recombinantly. The specification fails to provide enablement in the form of guidance in determining how to effectively make the claimed antibodies, through appropriate analysis and expression of the gene products, ie. the use of appropriate expression systems and expression conditions.

Claims 11,13 and 15 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Applicant has amended the claims by removing the tat gene product which was shown to be expressed from split open reading frames. This however, is insufficient to enable the claimed invention, as the disclosure provides no teaching of the intricacies involved with HIV peptide expression. At the time the invention was made, there was little known about HIV and even less about gene products related to HIV. It would have been undue experimentation in order to make gene products which would yield diagnostically useful antibodies as intended by the specification. (see above discussion)

Applicant has submitted two papers in attempt to establish that identification and expression of ORFs was well known in the art. The first, Maniatis, deals with cDNA cloning of transcribed genomic DNA of eukaryotic cells. HIV is a virus which has open reading frames which are overlapping and therefore, may produce proteins quite differently from cDNA reverse transcribed from animals cell extracts. This procedure enables one of ordinary skill in the art to make proteins from the DNA of animal cells if the protein can predictably yield a functional protein. The second reference teaches the identification of ORFs. Of course, two things should be noted here. First, the method taught here would be expected work with proteins obtained from a single ORF, but may not be effective in identifying proteins from multiple ORFs. Second, even if one were able to make the gene product from the desired ORF, one could not predict that these proteins would elicit antibodies which are detectable in sera. The fact that a gene product is expressed, does not automatically lead one of ordinary skill in the art to the conclusion that diagnostic antibodies would be produced. There was no predictability in detecting HIV by using any of the ORF products claimed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or

on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11,13 and 15 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kalyanarman or Schupbach et al. as evidenced by Arya et al., Wong-Staal and Cohen et. al..

The claims are drawn to an isolated antibody which binds with a peptide of HIV-1 having specific sequences. The language "isolated" has been interpreted to read on antibodies or anti-sera which is separated from the body. The language "having" has been interpreted as open claim language.

The two references teach the analysis of HTLV-III (renamed HIV-1) in infected individuals. In Schupbach et al. the authors analyze HTLV-III using antibodies in serum of infected individuals. This analysis leads to the detection of specific antigens of varying molecular weight. Since the serum of infected individuals contains a wide spectrum of antibody specificities, and since the ORFs of the HIV are expressed proteins, than inherently, the antibodies found in the serum of HIV infected individuals, would have specificities toward the ORFs as identified in the claims. This is clearly evidenced by Arya who teach the immune reactivity of infected sera with protein *vif* (ORF-Q) and *nef* (ORF-R), Wong-Staal et al. who teach the prevalence of antibodies specific for *vpr* (ORF-1) and Cohen et al. who teach antibodies in human sera which precipitate *vpu* (ORF-4).

A similar logic applies to Kalyanaraman. The fact that the references were not looking for antibodies to the ORFs does not detract from the fact that these antibodies were actually present in the serum of the HIV infected patients, which serum was isolated from the host.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lila Feisee whose telephone number is (703) 308-2731. The examiner can normally be reached on Mondays-Fridays from 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Lacey, can be reached on (703) 308-3535. The fax number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Feisee/tf

March 8, 1995
March 21, 1995

LILA FEISEE
PATENT EXAMINER
GROUP 1800